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Review Article

Efficacy of coronary CT angiography: Where we are, where we are going, and where we want to be

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Abstract. Over the decade since its earliest introduction, coronary CT angiography has spread rapidly, despite the fact that its validation base is smaller than that of alternative imaging examinations. Consensus statements have issued a call for improvement of coronary CT angiography's knowledge base. This article reviews recent progress in validating the efficacy of coronary CT angiography in the detection of coronary artery disease, with a focus on clinical decision making, management, and outcomes. We discuss the rationale for comparative effectiveness research and a framework for assessment of levels of efficacy. Comparison is made with radionuclide myocardial perfusion imaging, which serves as a model noninvasive examination. The potential roles of coronary CT angiography in screening, early triage, and as a gatekeeper for catheterization are discussed. Although few randomized controlled trials have been performed to date, we review the pivotal publications and mention ongoing and future efforts. Cardiovascular event rates provide the basis for estimating the success of potential study designs. The rigorous validation of coronary CT angiography may serve as a model for other noninvasive diagnostics.

Introduction

Cardiovascular disease is both the leading cause of death in industrialized countries and the medical condition responsible for the greatest health care expenses. Between 1995 and 2005 there was a decrease in the rate of cardiovascular disease mortality of approximately 25%.[1] This has been attributed to advances in risk factor modification and earlier diagnosis combined with aggressive pharmacotherapy and invasive treatment. Our focus, diagnosis, involves a variety of clinical and noninvasive imaging algorithms. Noninvasive diagnostics have the unfortunate dual challenge of being particularly difficult to rigorously assess in randomized controlled trials[2] and are most often scrutinized by policy makers and payers.[3] Detection of coronary artery disease is well studied, yet outcomes-based evidence is lacking even for traditional methods such as radionuclide myocardial perfusion imaging.[4] Recent attention to comparative effectiveness and radiation safety has resulted in rigorous scrutiny of coronary CT angiography. In 2006, when the initial coronary CT angiography appropriateness criteria were published, the modality was an "evolving field with limited evidence."[5] We describe progress in coronary CT angiography efficacy research ("where we

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are"), highlight the focus of current efforts of investigation ("where we are going"), and explain why we are not yet "where we want to be."

Efficacy and levels of evidence

We briefly define key terms necessary to understand the assessment of efficacy. Diagnostic accuracy (also called diagnostic efficiency) refers to the level of agreement between the test under evaluation and a trusted reference standard. In the case of coronary CT angiography, the reference standard is usually conventional angiography. Efficacy is the performance of a test or intervention under ideal circumstances (eg, when performed by an expert or in a specialized center). Effectiveness refers to the performance of a test under usual clinical conditions. Early studies of a new technology, such as coronary CT angiography, almost invariably assess efficacy rather than effectiveness. The cost-effectiveness of a procedure or diagnostic test expresses the ratio of the benefits of the test to the cost it entails.

The May 2009 comparative effectiveness research consensus statement from the American Heart Association assessed noninvasive imaging modalities similarly to treatment-based interventions.[6] This sentiment is echoed by the National Heart, Lung, and Blood Institute.[7] Treatment-based interventions are traditionally evaluated by multicenter randomized controlled trials that measure reductions in major adverse cardiovascular events. In contrast, after an imaging modality is developed, diagnostic accuracy is the primary metric. Although diagnostic accuracy may be a prerequisite for efficacy, it may not translate into better patient outcomes.

Some have argued that, in the case of coronary artery disease, demonstration of high diagnostic accuracy should be sufficient because treatment of coronary disease leads to improved clinical outcomes. If the accuracy of coronary CT angiography surpasses that of more traditional modalities, such as myocardial perfusion imaging, then improved outcomes would be a given, based on the premise that better detection will lead to earlier and more successful treatment. This logic often fails for diagnostic imaging because 2 modalities rarely, if ever, detect the same spectrum of disease. Hence, randomized clinical trials remain necessary to show an outcomes benefit.[8]

The largest prospective study (n = 517) comparing coronary CT angiography and radionuclide stress myocardial perfusion imaging exemplified the different spectra of disease shown by 2 imaging modalities. Coronary CT angiography had a calculated positive predictive value of 53% for a significant scintigraphic abnormality, whereas myocardial perfusion imaging had a 49% positive predictive value for obstructive coronary disease on CT angiography.[9] Thus, if either coronary CT angiography or radionuclide perfusion were abnormal, the odds of the alternate modality following suit were no better than a coin flip. Although the major event rates were similar for patients with abnormal CT angiography or perfusion imaging, outcomes research is needed to show benefits from treatment for patients identified by each modality.

Unfortunately for coronary CT angiography, as with much of clinical medicine, well-designed randomized controlled trials with clinical outcome endpoints are not yet available to guide decision making. Therefore, current practice is based on less-rigorous retrospective and prospective observational studies that have not focused on major clinical outcomes, but, instead, assess lower forms of efficacy. We have modified a 6-tiered description of levels of efficacy from a National Council on Radiation Protection and Measurements working committee[10] (Table 1) to assess published studies and to highlight areas of strength and weakness in the validation of coronary CT angiography.

Trial paradigms

This review is organized by using 4 clinical trial paradigms: (1) screening asymptomatic patients who may or may not have one or more cardiovascular risk factors, (2) early triage of patients who present acutely to the emergency department to facilitate and streamline subsequent care, (3) first gatekeeper for coronary catheterization to select the most likely subgroup to benefit from invasive workup, and (4) second gatekeeper for catheterization to identify candidates for revascularization and to exclude patients who can safely avoid diagnostic angiography from the group that is traditionally catheterized. The likelihood of coronary disease generally increases from paradigm 1 through 4. Obstructive coronary artery disease is uncommon in unselected asymptomatic patients and is present in a majority of patients who would usually undergo cardiac catheterization.

Screening

Many people who have a major cardiovascular event do not have prior symptoms.[11] The incidence of severe, asymptomatic coronary artery disease is higher in certain groups such as women and patients with diabetes, renal disease requiring dialysis, and cerebrovascular or peripheral arterial disease. Framingham risk calculation, C-reactive protein concentrations, and coronary artery calcium scoring have proven useful in risk stratification. Even so, a method to detect patients with obstructive coronary disease who might benefit from revascularization is of clinical importance. Coronary CT angiography has been suggested for this role[11]; however, the radiation burden inherent to CT[12] and a lack of validation has limited enthusiasm for this approach.

Several studies have assessed the feasibility of screening coronary CT angiography in unselected volunteers,[11] those with one or more risk factors for coronary disease,[13–16] type 2 diabetics,[14,17,18] and women.[19] For the most part these